



INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

| | | | |
|--|--|---|-----------------------|
| Applicant's or agent's file reference Case 22225 WO | FOR FURTHER ACTION | | See Form PCT/IPEA/416 |
| International application No. PCT/EP2004/012058 | International filing date (day/month/year) 26.10.2004 | Priority date (day/month/year) 07.11.2003 | |
| International Patent Classification (IPC) or national classification and IPC C07C67/08, C07C69/017, C07C69/16, C07D311/72 | | | |
| Applicant DSM IP ASSETS B.V. et al. | | | |
| <p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 4 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input checked="" type="checkbox"/> sent to the applicant and to the International Bureau) a total of 1 sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p> | | | |
| <p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input checked="" type="checkbox"/> Box No. VIII Certain observations on the international application</p> | | | |
| Date of submission of the demand 02.06.2005 | | Date of completion of this report 15.03.2006 | |
| Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465 | | Authorized Officer Herz, C Telephone No. +49 89 2399-8275  | |

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/EP2004/012058

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

Description, Pages

1-5 as originally filed

Claims, Numbers

1-7 received on 08.09.2005 with letter of 05.09.2005

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):

* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/EP2004/012058

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | |
|-------------------------------|-------------|-----|
| Novelty (N) | Yes: Claims | 1-7 |
| | No: Claims | |
| Inventive step (IS) | Yes: Claims | 1-7 |
| | No: Claims | |
| Industrial applicability (IA) | Yes: Claims | 1-7 |
| | No: Claims | |

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

**INTERNATIONAL PRELIMINARY
REPORT ON PATENTABILITY
(SEPARATE SHEET)**

International application No.

PCT/EP2004/012058

1. Due to the invariable use of methane trisulfonic acid as an reaction catalyst the process claimed is considered to be novel vis-à-vis the state of the art as represented by the documents cited in the International Search Report (ISER).

With regard to significantly improved yields using markedly lower amounts of catalyst the a surprising improvement has been demonstrated being indicative of an inventive solution of the technical problem of providing compounds exhibiting a significantly improved insulin level lowering activity (Art. 33 (3) PCT).

2. With regard to the term "ketoisophorone" the claims are not fully supported by the description wherein the term "3,5,5-trimethyl-1,4-benzoquinone" is recited (Art. 6 PCT).

What is claimed is:

- 5 1. Process for the preparation of 2,3,5-trimethyl-1,4-hydroquinone diacylates by reacting ketoisophorone with an acylating agent in the presence of methane trisulfonic acid.
2. A process as in claim 1 wherein the reaction is carried out in the presence of about 0.01 mol% to about 2 mol% of methane trisulfonic acid, based on ketoisophorone.
- 10 3. A process as in claim 2 wherein the reaction is carried out in the presence of about 0.1 mol% to about 1 mol% of methane trisulfonic acid, based on ketoisophorone.
4. A process as in any one of claims 1-3 wherein the molar ratio of acylating agent to
15 ketoisophorone is about 10 to 1, preferably about 3 to 1.
5. A process as in any one of claims 1-4 wherein the acylating agent is acetic anhydride.
6. A process as in any one of claims 1-5 wherein the reaction is carried out at about 0 °C to
20 about 140 °C, preferably at about 20 °C to about 70 °C.
7. A process as in any one of claims 1-6 wherein the 2,3,5-trimethyl-1,4-hydroquinone diester obtained is converted in a manner known per se to α -tocopherol.
